

Application No. 10/597,636  
AMENDMENT dated March 8, 2011  
Reply to Office Action of November 9, 2011  
Attorney Docket 9248-88834-US

**REMARKS**

Claims 15, 17-23, 25, 26 and 32-39 stand rejected. Claims 1-14 and 16 were previously canceled while claims 24-25 and 27-31 were previously withdrawn. Claims 14, 17, 18, 20, 21, 26 and 36 have been amended while claim 25 has been canceled herein. Further, new claim 40 has been added herein. Therefore, claims 15, 17-23, 26, and 32-40 are pending and at issue. Applicants respectfully request reconsideration of the rejections and allowance in light of the foregoing amendments and the following remarks herein.

***Claim Rejections Under 35 U.S.C. § 112***

Claims 15, 17-23, 25, 26 and 32-39 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter. Applicants have amended many of the claims and present the following comments.

Claim 15 stands rejected regarding alleged antecedent basis for “the cell activation status.” Applicants have amended the claim to recite “the neutrophil cell activation status” as suggested by the Examiner.

Claim 15 stands rejected regarding “the enzyme” when compared to “the active enzyme” as recited in the preamble. Applicants would like to point out that the phrases are referring to two different features, “the enzyme” referring to the total enzyme, and “the active enzyme” which refers just to the active enzyme, not the total enzyme. Therefore, one skilled in the art would be able to readily understand the differences between these recited features.

Claim 15 stands rejected for allegedly omitting essential steps. Claim 15 has been amended to recite the step of immunocapturing the enzyme present in the biological sample by contacting the biological sample with an enzyme specific polyclonal or monoclonal antibody. Further, claim 15 has been amended to clarify that detecting and/or measuring

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active enzyme present in the biological sample indicates the activation status of neutrophil cells in the biological sample. Therefore, claim 15 is not incomplete.

Claim 17 stands rejected for allegedly failing to recite positive method steps. Claim 17 has been amended to clarify “washing to remove...” and “adding a specific substrate...” Applicants assert that claim 17 does recite positive method steps such that this rejection should be withdrawn.

Claim 17 stands rejected regarding the phrase “the enzyme.” As discussed above with respect to claim 15, “the enzyme” refers to the total enzyme (active and inactive) whereas “the active enzyme” refers just to the active enzyme. Claim 17 refers to “the enzyme” which would be readily understood by those skilled in the art when read in the context of the entire claim including claim 15, from which claim 17 depends.

Claim 17 stands rejected regarding the “washing step.” Applicants assert that one skilled in the art would readily understand washing to remove any components that can interfere with the measurement of the enzyme activity, as found in amended claim 17.

Claim 18 stands rejected regarding “a substrate of fluorimetric reaction product” in view of “a specific substrate” as found in claim 17. Claim 18 has been amended to recite that “the substrate is a fluorimetric reaction product.” Therefore, this phrasing would be clear to those skilled in the art.

Claim 18 stands rejected for allegedly lacking antecedent basis for “the reaction medium.” Claim 18 has been amended to delete this language.

Claim 20 stands rejected for alleged improper antecedent basis for “a neutrophil activation status.” Claim 20 has been amended to recite “the neutrophil cell activation status.”

Claim 21 stands rejected for allegedly lacking antecedent basis for the phrase “the enzyme values.” Claim 21 has been amended as suggested by the Examiner to recite “the active enzyme values.”

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Claim 21 stands rejected as allegedly being vague regarding a number of phrases recited therein. Claim 21 has been amended to clarify the allegedly vague phrases.

Claim 21 stands rejected for allegedly lacking antecedent basis for a number of phrases. Claim 21 has been amended to clarify these alleged antecedent basis problems.

Claim 23 stands rejected for allegedly being vague regarding the term "effective." Applicants assert that the phrase "an effective amount of nitrile" would be understood in view of the claim when read in its entirety. Further, the specification adds further details which would permit one skilled in the art to readily understand the phrase.

Claim 25 is rejected as allegedly being indefinite. Applicants note that claim 25 has been canceled herein and therefore is no longer at issue.

Claim 26 stands rejected as allegedly being indefinite. For example, the Office Action notes that the phrase "comprising the necessary elements for" provides an intended result. Claim 26 has been amended to remove this phrase. Further, claim 26 has been amended to recite "antibodies effective for immunocapturing" and "a substrate effective for detecting and/or measuring." Therefore, claim 26, as amended, recites specific physical features of the kit or device.

Claims 32-34 stand rejected for allegedly lacking antecedent basis for the phrase "the enzyme." As discussed above with respect to claim 15, "the enzyme" is different from "the active enzyme" as found in the claims. Further, proper antecedent basis exists for "the enzyme" such that this rejection should be withdrawn.

Claim 36 stands rejected for allegedly lacking antecedent basis for the phrase "quantifying enzyme level." Claim 36 has been amended to recite "comparing and correlating the quantified active enzyme level with a standard active enzyme curve" similar to the proposal by the Examiner. Therefore, this claim is clear and has proper antecedent basis for the features recited therein.

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Claims 37-39 stand rejected for allegedly lacking antecedent basis for the phrase "the enzyme." As discussed above with respect to claim 15, "the enzyme" is different from "the active enzyme" as found in the claims. Further, proper antecedent basis exists for "the enzyme" such that this rejection should be withdrawn.

Therefore, Applicants assert that the rejections under § 112 have been either overcome or rendered moot such that this rejection should be withdrawn.

*Claim Rejections Under 35 U.S.C. § 102*

Claims 25, 26 and 37 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,460,961 to Deby et al. Applicants note that claim 25 has been canceled herein and is no longer at issue. Further, Deby et al. fails to disclose one or more features recited in claim 26, from which claim 37 depends such that this rejection should be withdrawn and the claims allowed.

Claim 26 recites a kit or device which specifically measures the active enzyme content only and includes a substrate effective for detecting and/or measuring active enzyme present in the biological sample. Deby et al., on the other hand, is directed to a completely different method in which the total myeloperoxidase (MPO), including active and inactive, is immunocaptured. The subsequent measurement in Deby et al. is indicative of the total MPO (active and inactive) as opposed to just the active enzyme as recited in claim 26.

The Office Action alleges that Deby et al. discloses MPO being contacted with active enzyme-specific antibody. However, contrary to the allegations in the Office Action, Deby et al. fails to disclose or suggest detection of the enzymatic activity of MPO bound to antibodies. Instead, Deby et al. describes at col. 21, lines 37-64 that alkaline phosphatase activity is measured which reflects the total MPO and not the active MPO.

A different method is described in Deby et al. at col. 23, line 64 through col. 22, line 14. This method detects MPO which is present in a reaction mixture and not that which is bound

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to antibodies. This method is unrelated to and otherwise not combinable with the method described in Deby et al. at col. 21, lines 37-64.

Further, the Office Action asserts that “the enzyme activity of the MPO is also assayed using O-dianisidine or orthophenylene diamine as substrate in the presence of hydrogen peroxide in the mixture.” P. 7, lines 17-19. However, as described above, when the enzymatic activity of MPO is measured in Deby et al., that occurs in a liquid medium without any antibody and thus without any immunocapture. This has nothing to do with the SIEFED method recited in claim 26 where the enzyme is first immunocaptured and then the activity of the captured enzyme is measured.

Contrary to the Office Action’s assertion, at no point does Deby et al. refer to active enzyme specific antibodies. Instead, Deby et al. is directed to the total MPO (active and inactive). Therefore, as Deby et al. fails to disclose or suggest one or more features recited in claim 26, from which claim 37 depends, this rejection should be withdrawn and the claims allowed.

#### *Claim Rejections Under 35 U.S.C. § 103*

Claims 15, 17-21, 23, 32 and 36 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 99/61907 to Hansel et al. in view of Deby et al. This rejection should be withdrawn as the cited references fail to disclose or suggest one or more features recited in the claims.

The Office Action asserts that “Hansel et al. provide that the method differentially measure active MPO enzyme content only.” P. 9, lines 5-6. However, this is a complete mischaracterization of the reference. Hansel et al. does not distinguish neutrophil peroxidase (myeloperoxidase) from eosinophil peroxidase and from that of other peroxidases present in lymphocytes. Additionally, Hansel et al. does not provide any enabling details as to how to

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differentiate between measurement of myeloperoxidase activity and eosinophil peroxidase activity.

On page 6, lines 12-14 and page 7, lines 1-3, Hansel et al. presents information regarding the evolution of myeloperoxidase and eosinophil peroxidase with time according to the groups of subjects, but an isolation of the cell populations has been performed previously. Therefore, Hansel et al. does not disclose or suggest how to distinguish between the enzyme activities without a prior cell separation.

Therefore, for the reasons stated above, the Office Action's characterization of Hansel et al. is inaccurate and by itself illustrates a number of additional deficiencies found in the reference.

The Office Action also acknowledges that Hansel et al. fails to disclose or suggest contacting the biological sample with polyclonal or monoclonal antibodies that are specific for the active MPO so as to specifically capture the active enzyme MPO. To overcome this deficiency, the Office Action proposes combining Deby et al. with Hansel et al.

However, as discussed above, Deby et al. fails to disclose or suggest such features. Specifically, Deby et al. fails to disclose or suggest active enzyme only and instead is directed to total enzyme (active and inactive). Therefore, even assuming that Deby et al. is properly combined with Hansel et al., the proposed combination fails to disclose or suggest contacting the biological sample with polyclonal or monoclonal antibodies that are specific for the active enzyme so as to specifically capture the active enzyme, in addition to the other deficiencies in Hansel et al. as discussed above. As Hansel et al. and Deby et al., when considered alone or in combination, fail to disclose or suggest one or more features recited in the claims, the rejection should be withdrawn and the claims allowed.

Claim 22 stands rejected as allegedly being unpatentable over Hansel et al. in view of Deby et al. and further in view of Deby-Dupont et al. As noted above, Hansel et al. and Deby et al. fail to disclose or suggest a number of different features recited in claim 15, from which

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claim 22 depends. For example, contrary to the Office Action's assertion, Hansel et al. fails to disclose or suggest the recited polyclonal or monoclonal antibodies and Deby et al. is directed to total enzyme and not active enzyme as recited in the claims. Deby-Dupont et al. adds nothing regarding these deficiencies. Therefore, as Hansel et al., Deby et al. and Deby-Dupont et al., when taken alone or in combination, fail to disclose or suggest one or more features recited in claim 22, this rejection should be withdrawn and the claim allowed.

Claims 38 and 39 stand rejected as allegedly being unpatentable over Deby et al. in view of Terao et al. As described above, Deby et al. fails to disclose or suggest one or more features recited in claim 26. Terao et al. fails to overcome these deficiencies. Therefore, as Deby et al. and Terao et al., when taken alone or in combination, fail to disclose or suggest one or more features recited in claims 38 and 39, this rejection should be withdrawn and the claims allowed.

Claims 33 and 34 stand rejected as allegedly being unpatentable over Hansel et al. in view of Deby et al. and further in view of Terao et al. As noted above, Hansel et al. and Deby et al. fail to disclose or suggest a number of different features recited in claim 15, from which claims 33 and 34 depend. For example, contrary to the Office Action's assertion, Hansel et al. fails to disclose or suggest the recited polyclonal or monoclonal antibodies and Deby et al. is directed to total enzyme and not active enzyme as recited in the claims. Terao et al. adds nothing regarding these deficiencies. Therefore, as Hansel et al., Deby et al. and Terao et al., when taken alone or in combination, fail to disclose or suggest one or more features recited in claims 33 and 34, this rejection should be withdrawn and the claims allowed.

Claim 35 stands rejected as allegedly unpatentable over Hansel et al. in view of Deby et al. and further in view of Wilson et al. As noted above, Hansel et al. and Deby et al. fail to disclose or suggest a number of different features recited in claim 15, from which claim 35 depends. For example, contrary to the Office Action's assertion, Hansel et al. fails to disclose or suggest the recited polyclonal or monoclonal antibodies and Deby et al. is directed to total

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enzyme and not active enzyme as recited in the claims. Wilson et al. adds nothing regarding these deficiencies. Therefore, as Hansel et al., Deby et al. and Wilson et al., when taken alone or in combination, fail to disclose or suggest one or more features recited in claim 35, this rejection should be withdrawn and the claim allowed.

The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,  
FITCH, EVEN, TABIN & FLANNERY

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